

# Photoangiolytic Laser Treatment of Recurrent Respiratory Papillomatosis: A Scaled Assessment

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**Summary: Objectives.** To investigate the effectiveness of unsedated office-based photoangiolytic laser surgery (UOLS) for treating recurrent respiratory papillomatosis (RRP) using the Derkay severity scale, Voice Handicap Index-10 (VHI-10), and Grade, Roughness, Breathiness, Asthenia, Strain (GRBAS) scale. Although previous studies examined the effect of UOLS on voice quality, few studies evaluated the effect on disease regression or used accepted and validated scales as outcome measures.

**Study Design.** Retrospective case series.

**Methods.** Charts were reviewed for patients who underwent UOLS for RRP (2007–2010). Twenty-one patients met the inclusion criteria. Nineteen patients underwent treatment with a 532-nm potassium titanyl phosphate laser and two with a 585-nm pulsed dye laser. The Derkay, VHI-10, and GRBAS scores of posttreatment findings were compared with those of the pretreatment findings.

**Results.** Twenty-one patients underwent 81 office procedures. Mean follow-up was 18 months. From baseline to latest follow-up, there was significant improvement in the mean Derkay score from 6.1 to 3.0 ( $P = 0.001$ ), VHI-10 score from 24.5 to 15.9 ( $P = 0.04$ ), and GRBAS score from 8.6 to 4.9 ( $P = 0.004$ ).

**Conclusions.** UOLS results in patient benefit from disease regression, reduced voice handicap, and improved voice quality without the risks associated with direct laryngoscopy and general anesthesia. UOLS is an effective, safe, non-experimental treatment modality for RRP that has shifted the therapeutic paradigm while decreasing patient morbidity.

**Key Words:** Recurrent respiratory papillomatosis–Derkay papilloma severity scale–GRBAS scale–Voice Handicap Index-10–Pulsed dye laser–KTP laser.

## INTRODUCTION

Recurrent respiratory papillomatosis (RRP) is a challenging condition for the clinician to treat. Traditionally, the disease has warranted repeated surgical procedures under general anesthesia. However, recent developments with photoangiolytic lasers have permitted patients with epithelial diseases of the larynx to be treated in the office through a flexible laryngoscope without the need for sedation. The 585-nm pulsed dye laser (PDL) was first described in 1998<sup>1</sup> as a novel modality for the treatment of RRP. The 532-nm potassium titanyl phosphate (KTP) laser has recently emerged in the treatment of RRP both in the office and in the operating room.<sup>2,3</sup> Photoangiolytic lasers selectively ablate the papilloma microvasculature with limited thermal injury to the surrounding tissue because of their selective absorption by oxyhemoglobin. A major advantage is that the laser allows preservation of epithelium with a reduced risk of tissue fibrosis and webbing that is associated with conventional CO<sub>2</sub> laser ablation.

The value of photoangiolytic lasers for the treatment of RRP is steadily being established in the literature.<sup>2,3</sup> However, few studies have used accepted and validated scales to evaluate

the effectiveness of photoangiolytic lasers. The purpose of this report was to assess the effectiveness of unsedated office-based photoangiolytic laser surgery (UOLS) on disease regression, voice handicap, and voice quality using such outcome measures.

## MATERIALS AND METHODS

A case series was reviewed retrospectively of patients undergoing UOLS for RRP under topical anesthesia from August 1, 2007, to August 1, 2010. The study was approved by the Institutional Review Board of the New York Eye and Ear Infirmary. Twenty-one patients fulfilling the inclusion criteria were identified from the laser log for the 585-nm PDL and 532-nm KTP laser. The inclusion criteria included patients with at least 12 months of follow-up and in-office treatment with a photoangiolytic laser. The office charts for the identified patients were reviewed. The severity of RRP for each office visit was staged retrospectively by reviewing the laryngoscopic images for all patients and grading the disease using the anatomical component of the Derkay severity score, the leading numerical staging system for RRP.<sup>4</sup> Staging was performed in an unblinded manner by the primary author who was not involved in the treatment of the patients. The Derkay severity score consists of an anatomical component, which designates a grade for the extent of the lesion at each site of the aerodigestive tract, and a clinical component, which was not used in our study. Each anatomical site is scored using a three-point scale, with zero denoting no visible lesion, one surface, two raised, and three a bulky lesion.

In addition, the Voice Handicap Index-10 (VHI-10) score and the Grade, Roughness, Breathiness, Asthenia, Strain (GRBAS) score assigned at the time of office visits were collected.<sup>5,6</sup> The VHI-10 is a measure of the level of handicap a patient

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experiences as a result of a voice disorder. The outcome measure ranges from 0 to 40, with a higher score showing an increased voice handicap. The GRBAS scale was developed as a perceptual analysis of voice quality for use by members of the voice clinic team. Voice quality is rated by five parameters: grade, roughness, breathiness, asthenia, and strain. Each parameter is assigned a score from 0 to 3 and summed to give a score out of 15. A higher score denotes more severe dysfunction. GRBAS scoring was performed in person at the time of the patient's office visit by any of the five speech-language pathologists who specialize in voice therapy at our institute or by the senior author. Disease regression was measured by comparing the baseline anatomical Derkay severity, VHI-10, and GRBAS scores at initial consultation with posttreatment findings at latest follow-up with a Mann-Whitney *U* test.

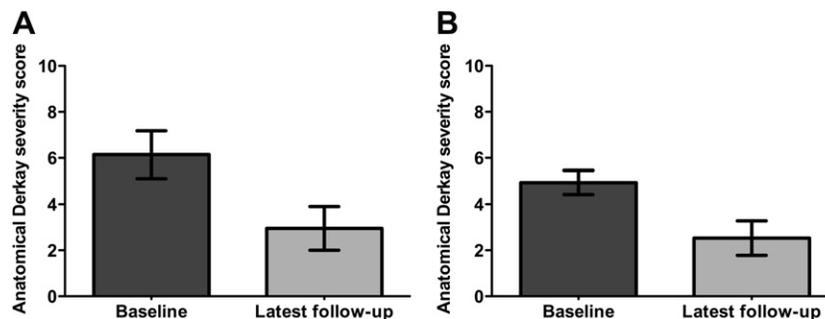
Twenty-one patients met the inclusion criteria. Diagnosis of RRP was confirmed by videostroboscopy and biopsy performed under topical or general anesthesia. All patients underwent initial treatment with CO<sub>2</sub> laser ablation of RRP under general anesthesia, with photoangiolytic laser therapy being used for treatment of recurrence. A 585-nm PDL (Candela Corporation, Wayland, MA) (pulse width of 450  $\mu$ s, 600–800 mJ per pulse, 0.6-mm fiber, and a working distance of contact to approximately 3 mm) was used for the first 13 treatments. After the acquisition of a 532-nm KTP laser (American Medical Systems, Minnetonka, MN) (pulse width of 15–20 ms, 20–40 W, 0.4-mm fiber, and a working distance of contact to 3 mm), the remaining 68 treatments were performed with this laser. The laser was delivered via a fiber passed through the working channel of a flexible distal chip transnasal esophagoscope (KayPENTAX, Lincoln Park, NJ). The procedure was performed in office on unsedated patients. Intranasal anesthesia was administered topically with 2% lidocaine hydrochloride and 0.125% phenylephrine hydrochloride. The larynx was anesthetized by dripping 4% lidocaine hydrochloride through the working channel of the laryngoscope. The treatment end point was defined by the blanching of the papilloma mucosa. For bulky lesions, the more superficial papilloma was ablated and debrided with the tip of the fiber exposing the deeper unaffected papilloma. The remaining papilloma was then treated until blanching. Patients were placed on 2–3 days of voice rest and

scheduled for follow-up office visit and laryngoscopy in 1 month. Patients received further UOLS for RRP as required based on their symptoms after recurrence and their effect on quality of life. The number of procedures was recorded for each patient.

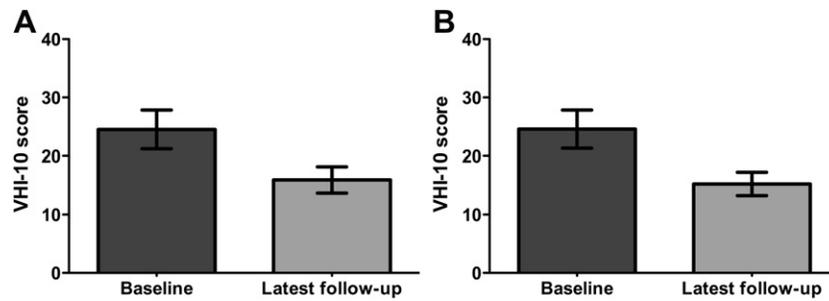
## RESULTS

Analysis of the laser log for the 585-nm PDL and 532-nm KTP laser revealed that 125 patients underwent 210 UOLS from August 1, 2007, to August 1, 2010, for a range of pathologies. Twenty-one patients aged 16–84 years (16 males and five females) underwent a total of 81 procedures for RRP. All patients were treated by the senior author (M.J.P.). Nineteen subjects underwent treatment with the 532-nm KTP laser and two with the 585-nm PDL. The mean number of procedures for each patient was 3.9 (range, one to eight procedures). No complications were encountered. Mean follow-up was 18 months (range, 12–40 months). All patients tolerated the procedure. No perioperative or postoperative complications were reported. Overall, 38.6% (81/210) of in-office photoangiolytic procedures performed at our institution were undertaken to treat RRP.

Anatomical Derkay severity scoring was performed for all subjects, and the mean baseline score at initial presentation was 6.1 (range, 2–18). As seen in Figure 1A, there was a statistically significant decrease in the anatomical component of the Derkay severity score at the latest follow-up after treatment when compared with baseline findings before treatment ( $P = 0.001$ ). The mean score at the latest follow-up was 3.0 (range, 0–9). All but two patients experienced an improvement in their anatomical Derkay severity score. These two patients had unchanged anatomical Derkay severity scores. Data for the VHI-10 were available for 15 subjects. Figure 2A shows that there was a statistically significant improvement from the baseline VHI-10 score at initial presentation (mean, 24.5; range, 4–38) to the latest follow-up (mean, 15.9; range, 2–33) ( $P = 0.04$ ). GRBAS scoring was performed for 16 subjects, and there was also a statistically significant improvement from baseline (mean, 8.6; range, 3–15) to the latest follow-up (mean, 4.9; range, 0–12) for all patients ( $P = 0.004$ ) as



**FIGURE 1.** Mean anatomical Derkay severity score for subjects at baseline and at latest follow-up (mean follow-up, 18 months) after UOLS for RRP. **A.** All patients treated with photoangiolytic laser. There was a significant improvement ( $P = 0.001$ ) in the anatomical Derkay severity score. **B.** Patients treated with photoangiolytic laser without cidofovir. There was a significant improvement ( $P = 0.0005$ ) in the anatomical Derkay severity score. Lower anatomical Derkay severity score indicates less severe disease. Error bars represent standard error of the mean.



**FIGURE 2.** Mean VHI-10 score for subjects at baseline and at latest follow-up (mean follow-up, 18 months) after UOLS for RRP. **A.** All patients treated with photoangiolytic laser. There was a significant improvement ( $P = 0.04$ ) in the VHI-10 score. **B.** Patients treated with photoangiolytic laser without cidofovir. There was a significant improvement ( $P = 0.03$ ) in the VHI-10 score. Lower VHI-10 score indicates less voice handicap. Error bars represent standard error of the mean.

demonstrated in Figure 3A. The typical patient response is seen in Figure 4.

Four patients received cidofovir as adjuvant treatment. One patient had severe disease and had been undergoing monthly resections via direct laryngoscopy under general anesthesia (DLGA) for the previous 12 months at an institution outside the United States before referral. Considering the severity of the disease and the need for significant travel for treatment, aggressive therapy with cidofovir was part of his initial treatment regimen at our institution. His GRBAS and Derkey severity scores reduced from 15 to 3 and 18 to 6, respectively. One patient had had papilloma for 20 years and had been undergoing DLGA since the age of 8 years. Although he had had a significant decrease in the bulk of his disease and had needed only two DLGAs since the institution of UOLS 3 years prior, he had persistent dysphonia (VHI-10, GRBAS, and Derkey severity score change from 40 to 36, 13 to 14, and 20 to 10, respectively). Cidofovir therapy was instituted in an attempt to optimize phonation with resultant VHI-10, GRBAS, and Derkey severity scores of 21, 6, and 8, respectively. Two patients with mild adult onset papilloma experienced improvement with the UOLS but had rapid recurrence of papilloma on the vibratory edge of the vocal fold, resulting in significant dysphonia despite the presence of mild disease and VHI-10, GRBAS, and Derkey severity scores of 33, 12, and 5 and 3, 2, and 2 before instituting cidofovir therapy. After treatment, the first patient's scores were

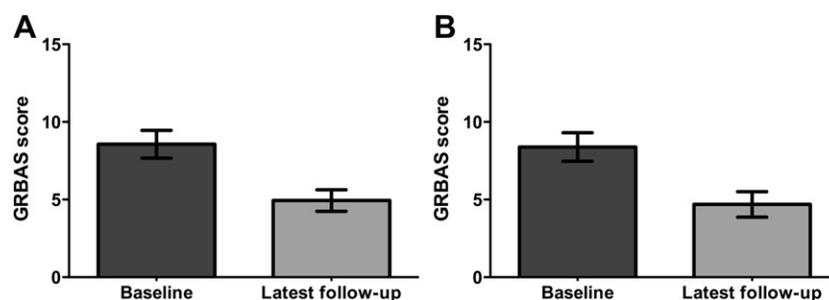
reduced to 5, 3, and 0, whereas the latter patient's scores were unchanged (Figure 5). Three of four of these patients experienced a dramatic reduction of the papilloma with four to five unsedated in-office injections of cidofovir occurring at 2-week intervals, occasionally in combination with UOLS. None of the patients required further DLGA for the treatment of papilloma.

Recognizing that the addition of adjuvant treatment with cidofovir might affect patients' ultimate outcome, the data were also reviewed after removing patients who had undergone this treatment. As shown in Figures 1B, 2B and 3B, patients treated with a photoangiolytic laser without cidofovir still experienced significant improvements in the mean Derkey score from 4.9 to 2.5, VHI-10 score from 24.6 to 15.3, and GRBAS score from 8.4 to 4.7 (respective  $P$  values of 0.0005, 0.03, and 0.004).

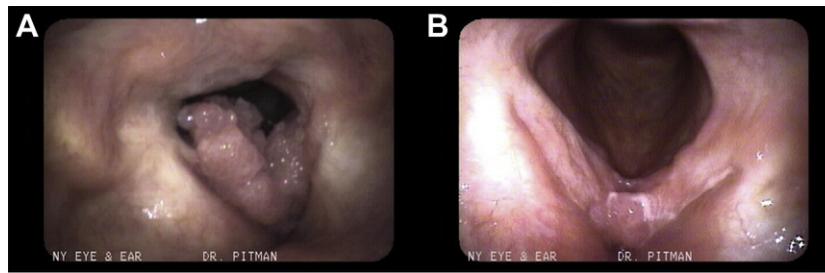
Only four of the 21 patients needed DLGA after UOLS was instituted in their therapy. Two of them were part of the cidofovir group. Three underwent only one further surgery.

## DISCUSSION

RRP is one of the most common benign tumors of the larynx, with an estimated incidence in the United States of 4.3 per 100 000 among the pediatric population and 1.8 per 100 000 among the adult population.<sup>7</sup> At present, no treatment has succeeded in curing RRP, and the mainstay of therapy is surgery to



**FIGURE 3.** Mean GRBAS score for subjects at baseline and at latest follow-up (mean follow-up, 18 months) after UOLS for RRP. **A.** All patients treated with photoangiolytic laser. There was a significant improvement ( $P = 0.004$ ) in the GRBAS score. **B.** Patients treated with photoangiolytic laser without cidofovir. There was a significant improvement ( $P = 0.004$ ) in the GRBAS score. Lower GRBAS score indicates better voice quality. Error bars represent standard error of the mean.



**FIGURE 4.** Typical response after KTP laser treatment. This patient's papilloma is contained to a minimum with intermittent KTP laser treatments every 6–18 months depending on the patient's symptoms.

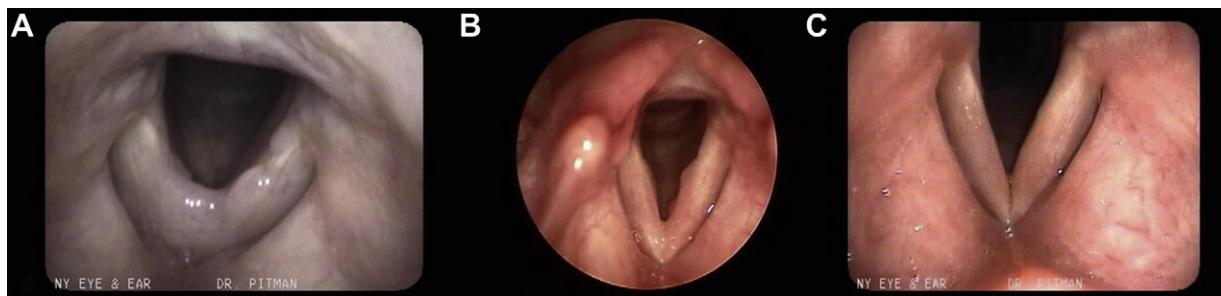
control the disease. The goals of the surgical management of RRP are to reduce disease severity, improve voice quality, and maintain a patent airway. They must be balanced with the morbidity caused by any intervention. The use of the 585-nm PDL to treat laryngeal papillomas under general anesthesia was first described by McMillan et al.<sup>1</sup> The authors noted that the vocal fold mucosa appeared to be uninjured. In 2004, Zeitels et al<sup>8</sup> demonstrated that unsedated in-office 585-nm PDL treatment for RRP was a valuable treatment modality. The same group subsequently introduced 532-nm KTP laser treatment in the office setting in 2006.<sup>2</sup> The 532-nm KTP laser has a longer pulse width than the 585-nm PDL, and its wavelength is better absorbed by oxyhemoglobin. Hence, it is hypothesized to cause less collateral thermal injury with better vascular coagulation.

A fundamental difference between the present study and previous studies is the use of accepted and validated outcome measures to demonstrate the effectiveness of UOLS. Subjects showed significant improvements in three accepted outcome measure scores at the latest follow-up after treatment with the 585-nm PDL or 532-nm KTP photoangiolytic laser. A decrease in the severity of RRP was apparent as measured by the anatomical Derkay severity score. There was an improvement in the subjects' perception of their voice handicap as measured with the VHI-10, which parallels the findings by Mouadeb and Belafsky.<sup>9</sup> A significant improvement in the subjects' voice quality was also demonstrated as judged by the voice clinic team using the GRBAS scale. Although most patients improve with photoangiolytic laser treatment alone, occasionally adjuvant therapy will be used to optimize the result. These injections may be performed in the office and appear to result in further

improvement in the outcome measures. In this study, three-fourths of the patients who received cidofovir experienced additional benefit when compared with laser treatment alone.

There were no complications in our study. None of the subjects in this study treated for RRP at the anterior commissure developed a web, and this complication has not been described in previous reports of photoangiolytic laser treatment of RRP. The risk of vocal fold scar development or anterior commissure web formation after photoangiolytic laser surgery is minimal. In contrast, Dedo and Yu<sup>10</sup> reported anterior glottic web formation in 27% of 244 patients undergoing conventional CO<sub>2</sub> laser treatment. The low complication rate can be attributed to the principle that underlies the way in which photoangiolytic lasers work. The wavelengths of photoangiolytic lasers are preferentially absorbed by oxyhemoglobin resulting in targeted photo-coagulation of the papilloma microvasculature. This allows epithelial preservation with reduced scarring of the superficial lamina propria and minimal thermal damage to the surrounding areas. The two major advantages of photoangiolytic laser therapy are the ability to treat anterior commissure disease without causing webbing and the ability for the procedure to be performed in the office without the risks associated with direct laryngoscopy and general anesthesia. Our findings are in agreement with other studies, which also support the safety of the 585-nm PDL and 532-nm KTP laser.<sup>2,3,8,9,11</sup> In addition, it has been shown that patients prefer in-office laser treatment over conventional therapy and there is a saving of \$5000.00 per case to the health care system.<sup>12,13</sup>

The advent of in-office unsedated photoangiolytic therapy for RRP has shifted the paradigm for the treatment of RRP.



**FIGURE 5.** A. Initial presentation with VHI-10, GRBAS, and Derkay severity scores of 33, 12, and 7, respectively. B. After KTP treatment with multiple recurrences at the vocal fold vibratory edge and corresponding scores of 33, 12, and 3. C. One year after adjuvant treatment with cidofovir with corresponding scores of 5, 3, and 0.

Because of the risks posed by direct laryngoscopy and general anesthesia, traditionally patients waited until their symptoms of dysphonia or dyspnea were severe before electing to have surgery. As such, patients endured significant chronic morbidity from RRP. Because of the efficacy, safety, decreased morbidity, and convenience of UOLS, the threshold for surgical intervention has been lowered. Patients are now treated when symptoms are interfering with their quality of life and activities of daily living, well before they are severe. Patients can be followed up and treated in a single office visit, returning to work the same day. Consequently, UOLS has shifted the paradigm of treatment to allow the surgeon and patient to “stay ahead” of the disease. As a result, not only is UOLS less morbid but so is RRP itself because there is no longer the need to tolerate persistent dysphonia and dyspnea.

Our study was subjected to several limitations including the inherent limitations of a retrospective review. Some patients underwent direct laryngoscopy and excision of RRP before referral to our institution. Vocal fold changes from these surgeries may decrease our ability to optimize the voice. The unpredictable relapsing and remitting natural history of RRP is a challenge for any study of RRP treatment efficacy. Derkay staging of RRP severity for each patient was performed in an unblinded manner, which may have been a source of bias in this study. Finally, it was not possible to obtain a complete set of VHI-10 and GRBAS scores for six and five patients, respectively.

## CONCLUSIONS

The present study demonstrates that UOLS is a safe and nonexperimental treatment modality that is highly effective in controlling RRP. Patients benefit from disease regression, reduced voice handicap, and improved voice quality as measured via accepted and validated outcome measures. This in-office unседated procedure is well tolerated and allows patients to be treated with minimal risk and morbidity and at a lower cost than DLGA. Because of UOLS, the treatment paradigm

for RRP has shifted to allow the surgeon and patient to stay ahead of the disease, which we believe decreases the morbidity of RRP.

## REFERENCES

1. McMillan K, Shapshay SM, McGilligan JA, Wang Z, Rebeiz EE. A 585-nanometer pulsed dye laser treatment of laryngeal papillomas: preliminary report. *Laryngoscope*. 1998;108:968–972.
2. Zeitels SM, Akst LM, Burns JA, Hillman RE, Broadhurst MS, Anderson RR. Office-based 532-nm pulsed KTP laser treatment of glottal papillomatosis and dysplasia. *Ann Otol Rhinol Laryngol*. 2006;115:679–685.
3. Burns JA, Zeitels SM, Akst LM, Broadhurst MS, Hillman RE, Anderson R. 532 nm pulsed potassium-titanyl-phosphate laser treatment of laryngeal papillomatosis under general anesthesia. *Laryngoscope*. 2007;117:1500–1504.
4. Derkay CS, Malis DJ, Zalzal G, Wiatrak BJ, Kashima HK, Coltrera MD. A staging system for assessing severity of disease and response to therapy in recurrent respiratory papillomatosis. *Laryngoscope*. 1998;108:935–937.
5. Rosen CA, Lee AS, Osborne J, Zullo T, Murry T. Development and validation of the voice handicap index-10. *Laryngoscope*. 2004;114:1549–1556.
6. Hirano M. *Clinical Examination of the Voice*. New York, NY: Springer-Verlag; 1981:81–84.
7. Derkay CS. Task force on recurrent respiratory papillomas. A preliminary report. *Arch Otolaryngol Head Neck Surg*. 1995;121:1386–1391.
8. Zeitels SM, Franco RA Jr, Dailey SH, Burns JA, Hillman RE, Anderson RR. Office-based treatment of glottal dysplasia and papillomatosis with the 585-nm pulsed dye laser and local anesthesia. *Ann Otol Rhinol Laryngol*. 2004;113:265–276.
9. Mouadeb DA, Belafsky PC. In-office laryngeal surgery with the 585nm pulsed dye laser (PDL). *Otolaryngol Head Neck Surg*. 2007;137:477–481.
10. Dedo HH, Yu KC. CO(2) laser treatment in 244 patients with respiratory papillomas. *Laryngoscope*. 2001;111:1639–1644.
11. Franco RA Jr, Zeitels SM, Farinelli WA, Anderson RR. 585-nm pulsed dye laser treatment of glottal papillomatosis. *Ann Otol Rhinol Laryngol*. 2002;111:486–492.
12. Rees CJ, Halum SL, Wijewickrama RC, Koufman JA, Postma GN. Patient tolerance of in-office pulsed dye laser treatments to the upper aerodigestive tract. *Otolaryngol Head Neck Surg*. 2006;134:1023–1027.
13. Rees CJ, Postma GN, Koufman JA. Cost savings of unседated office-based laser surgery for laryngeal papillomas. *Ann Otol Rhinol Laryngol*. 2007;116:45–48.